

## **Generation of a High Throughput Screening System for Small Molecules that can Rescue Axonopathy**

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Familial Dysautonomia (FD) is a neurological disease with both developmental and degenerative aspects including axonopathy of peripheral nerves. FD results from a point mutation in the ELP1 gene, causing reduced levels of the corresponding protein that functions in assembling a highly conserved, six-subunit complex known as Elongator. Elongator catalyzes the chemical modification of transfer RNAs needed for the translation of codon-biased transcripts that preferentially use AA- or AG-ending codons. Like FD, axonopathies are a common feature of many other neurological diseases including amyotrophic lateral sclerosis (ALS), and Alzheimer's. Despite their prevalence in neurodegenerative diseases, the discovery of therapeutics for treating axonopathies has been impeded by the difficult and costly nature of culturing primary neurons. Therefore, an experimental model that can withstand the manipulation required for a high throughput small molecule screen is essential for drug discovery. *Candida albicans* shows a pronounced polarized growth phenotype that is distinct among other yeasts. To determine whether this phenotype is dependent on Elongator, as is polarized growth in neurons, we made a *C. albicans* Elp1 knockout. Importantly, this knockout exhibits a severely compromised growth habit. Our long-term goal is to use this knockout to develop a high throughput screen for small molecules that can rescue normal polarized growth. Molecules that rescue in our yeast model system, will then be tested in vitro for the ability to rescue axon elongation in Elp1 deficient neurons.